REMARKS

Examiner Interview

Applicant wishes to thank the Examiner for the courtesy extended to the undersigned in the interview of April 7, 2009. The Examiner's Interview Summary mailed April 9, 2009 satisfactorily describes the substance of the interview.

Status of the Claims

Claims 1-28, 32-39, 42-48, 52, 54-64, 69 and 72-101 are pending herein.

Claims 32, 33, 80-83 and 87-89 have been rejoined. Thus, claims 4, 7, 11, 14, 19-22, 24, 25, 58-60, 62, 72-75, 84 and 85 are presently withdrawn.

Double Patenting

Claims 1-3, 5, 6, 8-10, 12, 13, 15-18, 23, 26-28, 32--39, 42-48, 52, 54, 55, 61, 69, 76-83 and 90-101 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 5-19, 24-26 and 35-40 of U.S. Patent No. 6,884,435 to O'Hagan. This rejection and its supporting remarks are respectfully traversed.

For example, claim 1 of the present application is directed to microparticles comprising: (a) a biodegradable polymer; (b) a cationic surfactant; and (c) a first polynucleotide-containing species adsorbed on the surface of the microparticles, *wherein the adsorbed first polynucleotide-containing species constitutes at least 5 percent of the total weight of the microparticles, wherein the cationic surfactant is present during formation of the microparticles, and wherein no cationic surfactant removal step is conducted subsequent to formation of the microparticles.*

This claim, for example, the italicized portion thereof, is neither taught nor suggested by the claims of US 6,884,435.

The Examiner has asserted, *inter alia*, that the O'Hagan "specification discloses that the polynucleotide can constitute 5% or 0.1 to 10% of the total weight of the microparticle (column 14, lines 6-10) and that the microparticles comprise 0.1 to 10% or 0.5 to 2% cationic surfactant (column 13, lines 30-37)."

Citing MPEP 804, Applicant had previously noted that, when considering whether the invention defined in a claim of an application would have been an obvious variation of the

invention defined in the *claim* of a patent, the patent specification can be used as a dictionary *to learn the meaning of a term* in the patent claim, but that the disclosure of the patent may not be used as *prior art* for purposes of an obviousness-type double patenting rejection.

The Examiner had previously responded, urging that the patent specification was used to define the "microparticle characteristics" in order to determine whether the claimed invention is an obvious variation of the invention claimed O'Hagan and further urging that the Examiner used only those portions of the specification pertaining to the invention claimed in the patent. As authority, the Examiner has provided the following citation from MPEP 804 II B, which pertains to *In re Vogel,* 422 F.2d 438, 441-42, 164 USPQ 619, 622 (CCPA 1970) in which it was held that a certain portion of a the patent specification may be "considered" for an purposes of an obviousness-type double patenting analysis (emphasis added):

> Further, those portions of the specification which provide support for the patent claims may also be examined and considered when addressing the issue of whether a claim in the application defines an obvious variation of an invention claimed in the patent. *In re Vogel*....The court in *Vogel* recognized "that it is most difficult, if not meaningless, to try to say what is or is not an obvious variation of a claim," but that one can judge whether or not the invention claimed in an application is an obvious variation of ***an embodiment*** disclosed in the patent which provides support for the patent claim. According to the court, one must first "determine how much of the patent disclosure pertains to the invention claimed in the patent" because ***only "[t]his portion of the specification supports the patent claims and may be considered."*** The court pointed out that "this use of the disclosure is not in contravention of the cases forbidding its use as prior art, nor is it applying the patent as a reference under 35 U.S.C. 103, since only the disclosure of the invention claimed in the patent may be examined."

In this regard, the *Vogel* Court more fully explained its reasoning as follows [emphasis added]:

> The second analysis question is: Does any claim in the application define merely an obvious variation of an invention disclosed and claimed in the patent? In considering the question, the patent disclosure may not be used as prior art. *In re Boylan*, supra [392 F.2d 1017, 55 CCPA 1041 (1968)]; *In re Aldrich*, 398 F.2d 855, 55 CCPA 1431 (1968). This does not mean that the disclosure may not be used at all. As pointed out above, in certain instances it may be used as a dictionary to learn the meaning of terms in a claim. It may also be used as required to answer the second analysis question above. We recognize that it is most difficult, if not meaningless, to try to say what is or is not an obvious variation of a claim. A claim is a group of words defining only the boundary of the patent monopoly. It may not describe any physical thing and indeed may encompass physical things not yet dreamed of. How can it be obvious or not obvious to modify a legal boundary? ***The disclosure, however, sets forth at least one tangible embodiment within the claim,*** and it is less difficult and more meaningful to judge whether that thing has been modified in an obvious manner. It must be noted that this use of the disclosure is not in contravention of the cases forbidding its use as prior art, nor is it applying the

> patent as a reference under 35 U.S.C. § 103, since only the disclosure of the invention claimed in the patent may be examined.

Thus, the Court in *Vogel*, examined a "tangible embodiment" within the claim. The Court specifically refused, on the other hand, to consider generic portions of the specification:

> …We must now determine how much of the patent disclosure pertains to the invention claimed in the patent, which is a process to be performed with pork, to which all the patent claims are limited. The specification begins with certain broad assertions about meat sausages. These assertions do not support the patent claims. The patent claims recite "pork" and "pork" does not read on "meat." To consider these broad assertions would be using the patent as prior art, which it is not….

The present case is analogous. The O'Hagan patent claims recite an adsorbed "antigen comprising a polynucleotide" whereas column 14, lines 6-10 of the specification pointed out by the Examiner pertains to adsorbed "macromolecules". Just as "pork" does not read on "meat" (which is held in *Vogel* to include pork), an "antigen comprising a polynucleotide" does not read on a "macromolecule". To consider the broad assertions regarding macromolecules in O'Hagan would be to improperly use O'Hagan as prior art.

Similarly, the O'Hagan patent claims recite a "cationic detergent" whereas column 14, lines 6-10 of the specification pointed out by the Examiner pertains to "detergent". As above, to consider the broad assertions regarding detergents in the specification would be to improperly use the O'Hagan patent as prior art.

The Examiner has responded in the Office Action of December 23, 2008 by alleging as follows. (1) The disclosure in the '435 patent on which the Examiner relied in making the obviousness-type double patenting rejection is not a generic portion with which the specification begins and where the specification makes broad assertions about macromolecules and detergents. (2) The teachings of the macromolecule constituting 5% of the total weight of the microparticle and of the microparticles as comprising 0.1 to 10% or 0.5 to 2% detergent specifically define the microparticles recited in the patent, which microparticles constitute a tangible embodiment. (3) The patent specification defines that the macromolecule could be a polynucleotide and that the detergent could be a cationic detergent such as CTAB (column 5, lines 28-35 and 65-67) and therefore, the teachings of the macromolecule constituting 5% (column 14, lines 6-1 0) and of the microparticles comprising 0.1 to 10% or 0.5 to 2% detergent (column 13, lines 30-37) do pertain to polynucleotides and cationic detergents such as CTAB.

Applicant respectfully disagrees. While the assertions about macromolecules and detergents referred to by the examiner may not be positioned at the beginning of the specification, this is hardly a rational basis for distinguishing *In re Vogel.* Moreover, rather than constituting a "tangible embodiment" as urged by the Examiner, the teachings referred to are generic, pertaining to a macromolecule (as opposed to a polynucleotide) and a detergent (as opposed to a cationic detergent). The fact that the patent specification *elsewhere* states that the macromolecule could be a polynucleotide and that the detergent could be a cationic detergent such as CTAB as argued by the Examiner is perfectly analogous to *In re Vogel*, wherein the patent specification stated elsewhere that the meat could be pork. Thus, as "pork" does not read on "meat" in *Vogel*, a "polynucleotide" does not read on a "macromolecule", nor does a "cationic detergent" read on a "detergent". To consider the broad assertions regarding macromolecules and the broad assertions regarding detergents would therefore constitute using the O'Hagan patent as prior art.

During the interview of April 7, 2009, the Examiner clarified that it was her belief that the instant case is not analogous to *Vogel,* because *Vogel's* description contained teachings pertaining to the genus (meat) but not the species (pork). (O'Hagan's description, on the other hand, contains teachings pertaining to both genus (macromolecule, detergent) and species (polynucleotide, cationic detergent).)

The description of the patent in *Vogel* (US 3,124,462), however, pertains not only to meat products (see, e.g., col. 1, lines 24-69) but also to pork (see, e.g., col. 2, line 3 to col. 4, line 18). Accordingly, *Vogel* is on point, and O'Hagan's generic teachings in the specification pertaining to macromolecules may *not* be considered for purposes of an obviousness-type double patenting analysis based on the patent claims, which are directed to polynucleotides. Similarly, O'Hagan's generic teachings in the specification pertaining to detergents may *not* be considered for purposes of an obviousness-type double patenting analysis based on the patent claims, which are directed to cationic detergents.

For at least the above reasons, it is respectfully submitted that claim 1 is patentable over the claims of O'Hagan under the doctrine of nonstatutory obviousness-type double patenting. All other claims depend, directly or indirectly, from claim 1 and are patentable over the claims of O'Hagan for at least the same reasons.

With respect to rejoined claims 32, 33, 80-83 and 87-89 the Examiner argues that these claims are obvious variants of claims 1 and 16-18 of O'Hagan. The Examiner's assertions are respectfully traversed. For example, these claims depend from claim 1 and are thus patentable for at least the same reasons as claim 1 above.

Reconsideration and withdrawal of the outstanding nonstatutory obviousness-type double patenting rejection are requested.

Provisional Double Patenting

Various claims have been provisionally rejected under the judicially created doctrine of obviousness type double patenting as being unpatentable over certain claims of copending Application No. 11/113,861. This rejection is a *provisional* rejection. As noted in MPEP 804 I B (emphasis added):

> Occasionally, the Examiner becomes aware of two copending applications…that would raise an issue of double patenting ***if one of the applications became a patent***. … The merits of such a provisional rejection ***can*** be addressed by both the applicant and the Examiner without waiting for the first patent to issue.
>
> The "provisional" double patenting rejection should continue to be made by the examiner in each application as long as there are conflicting claims in more than one application unless that "provisional" double patenting rejection is the only rejection remaining in one of the applications.
>
> …
>
> ***If the "provisional" double patenting rejection in one application is the only rejection remaining in that application, the examiner should then withdraw that rejection*** and permit the application to issue as a patent, thereby converting the "provisional" double patenting rejection in the other application(s) into a double patenting rejection at the time the one application issues as a patent.

Here, the double patenting issue has not yet matured for rational argument (i.e., the copending application has not issued as a patent and the claims may be amended/cancelled in the future). Indeed, at a future time, the provisional double patenting rejection may be the only rejection remaining in the present application, in which case the rejection will be withdrawn in accordance with the provisions of MPEP 804.

The Examiner has responded by arguing that what may happen in the future is irrelevant. However, what may happen in the future is not irrelevant, because it is possible that Applicant might needlessly reduce the scope of its claims by prematurely addressing the provisional rejection.

Furthermore, Serial No. 11/113,861 is a continuation of Serial No. 09/581,772, which matured as O'Hagan above. Thus the arguments set forth above in connection with the double patenting rejection over O'Hagan are analogous to the present provisional double patenting rejection as well.

Claim rejection under 35 USC §102(e)—O'Hagan

Various claims are rejected under 35 USC §102(e) as being anticipated by O'Hagan et al. US 6,884,435 (O'Hagan) as evidenced by Thalhamer (Endocrine Regulations, 2001, 35:143-166). This rejection is respectfully traversed.

As indicated in MPEP 2131, for a claim to be anticipated:

> …"The identical invention must be shown in as complete detail as is contained in the ... claim." *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989). The elements must be arranged as required by the claim, but this is not an *ipsissimis verbis* test, i.e., identity of terminology is not required. *In re Bond*, 910 F.2d 831, 15 USPQ2d 1566 (Fed. Cir. 1990)….

Thus, rejections under 35 U.S.C. § 102 are proper only when the claimed subject matter is *identically* described in the prior art.

Independent claim 1 presently requires, *inter alia*, microparticles comprising (a) a biodegradable polymer; (b) a cationic surfactant; and (c) an adsorbed polynucleotide-containing species constituting at least 5 percent of the total weight of the microparticles, wherein the cationic surfactant is present during formation of the microparticles, and wherein no cationic surfactant removal step is conducted subsequent to formation of the microparticles.

Adsorbed Polynucleotide-Containing Species

As indicated above, claim 1 requires an adsorbed polynucleotide-containing species constituting at least 5 percent of the total weight of the microparticles

Dependent claim 27 further requires that the adsorbed polynucleotide-containing species constitute 10 to 30 percent of the total weight of the microparticles.

Dependent claims 28, 91 and 93 further require that the adsorbed polynucleotide-containing species constitute 10 to 20 percent of the total weight of the microparticles.

These loadings constitute elevated loading levels relative to those previously demonstrated. By increasing polynucleotide-containing species loading levels one can, *inter*

alia, reduce the amount of polymer that is administered to an animal (for a given dose of polynucleotide-containing species). See paragraph [0006] of the present specification.

No specific examples falling within the claimed range are disclosed by O'Hagan. Example 7 of O'Hagan describes pCMVgp120 ***DNA loads ranging from 0.84 to 2.36%*** with decreasing loading efficiencies ranging from 88% to 59%. These do not meet the at least 5% loadings claimed in claim 1 (broadest claim). In an attempt to address this point, the Examiner had previously urged that "the loading efficiency is not 100% and therefore, in order to achieve a loading of 5%, one would have to use more than 5% input polynucleotide." However, this is not at all clear, as loading efficiency was seen to decrease with increasing target load. Moreover, the present rejection is an anticipation rejection and thus pertains to what was actually done in O'Hagan, rather than what might or might not have been obvious in view of O'Hagan.

At column 14, lines 8-9, O'Hagan teaches that "macromolecules are added to the microparticles to yield microparticles with adsorbed macromolecules having a weight to weight ratio of from about 0.0001:1 to 0.25:1 macromolecules to microparticles, preferably, 0.001:1 to 0.1, more preferably 0.01 to 0.05." See col. 14, lines 6-10.

As an initial observation, it is noted that this particular teaching is directed to macromolecules, rather than polynucelotides as claimed.

The Examiner has argued that O'Hagan clearly defines that the macromolecule can be a polynucleotide (column 5, lines 65-67) and therefore, the disclosed ranges apply to polynucleotides. In support the Examiner urges that "the MPEP states that A REFERENCE THAT CLEARLY NAMES THE CLAIMED SPECIES ANTICIPATES THE CLAIM NO MATTER HOW MANY OTHER SPECIES ARE NAMED".

O'Hagan, however, has not clearly named the species in question, at least by the standards required for anticipation. In this regard, see *In re Arkley*, 455 F.2d 586, 587-88, 172 U.S.P.Q. 524, 526 (CCPA 1972) (A "reference must clearly and unequivocally disclose the claimed compound or direct those skilled in the art to the compound without *any* need for picking, choosing and combining various disclosures …") (Emphasis in the original.)

To arrive at the presently claimed invention, one of ordinary skill in the art would have to, *inter alia*, choose polynucleotide-containing species from among the numerous other macromolecules disclosed in O'Hagan. This choice would have to be based on teachings found

in different portions O'Hagan. Thus, the claimed composition cannot be said to correspond to a "species" named by O'Hagan.

Moreover, assuming that the ranges of O'Hagan are applied in their entirety to the entire range of species embraced by the term "macromolecules," the ranges described are not sufficiently specific to constitute anticipation under the statute and the case law. In this regard, the standard for anticipation is high:

> When the prior art ***discloses a range which touches *>or< overlaps the claimed range, but no specific examples falling within the claimed range are disclosed***, a case by case determination must be made as to anticipation. In order to anticipate the claims, the claimed subject matter must be disclosed in the reference with "sufficient specificity to constitute an anticipation under the statute." What constitutes a "sufficient specificity" is fact dependent. If the claims are directed to a narrow range, >and< the reference teaches a broad range, ** depending on the other facts of the case, it may be reasonable to conclude that the narrow range is not disclosed with "sufficient specificity" to constitute an anticipation of the claims. **>See, e.g., *Atofina v. Great Lakes Chem. Corp*, 441 F.3d 991, 999, 78 USPQ2d 1417, 1423 (Fed. Cir. 2006) wherein the court held that a reference temperature range of 100-500 degrees C did not describe the claimed range of 330-450 degrees C with sufficient specificity to be anticipatory. Further, while there was a slight overlap between the reference's preferred range (150-350 degrees C) and the claimed range, that overlap was not sufficient for anticipation. ***"[T]he disclosure of a range is no more a disclosure of the end points of the range than it is each of the intermediate points."*** *Id.* at 1000, 78 USPQ2d at 1424…

MPEP 2131.03 (emphasis added). The facts of the present case are analogous to those above, if not more favorable to Applicant.

As indicated above, no specific examples falling within the claimed range are disclosed by O'Hagan (Example 7 of O'Hagan describes pCMVgp120 DNA loads ranging from 0.84 to 2.36%).

With regard to the macromolecule ranges described in O'Hagan, the narrow range disclosed in O'Hagan discloses microparticles with adsorbed macromolecules having a weight to weight ratio of from 0.01:1 to 0.05:1 (i.e., ranging from 0.01:1 or 0.0.01/[1+0.01]=0.99 percent up to 0.05:1 or 0.05/[1+0.05]=4.76 percent). There is thus no overlap between the ranges of instant claims (in claim 1, the broadest claim pending, the polynucleotide-containing species constitutes at least 5 percent of the total weight of the microparticles).

The intermediate range disclosed by O'Hagan involves microparticles with adsorbed macromolecules having a weight to weight ratio of from 0.001:1 to 0.1:1 (i.e., ranging from (0.001:1 or 0.001/[1+0.001]=0.1 percent up to 0.1:1 or 0.1/[1+0.1]=9.1 percent). Thus, the

intermediate range (0.1 to 9.1 percent) overlaps the numerical range of claim 1 (polynucleotide-containing species constitutes at least 5 percent of the total weight of the microparticles), but not claim 27 (polynucleotide-containing species constitutes 10 to 30 percent of the total weight of the microparticles) or claims 28, 91 and 93 (polynucleotide-containing species constitutes 10 to 20 percent of the total weight of the microparticles).

The broad range disclosed by O'Hagan involves microparticles with adsorbed macromolecules having a weight to weight ratio of from 0.0001:1 to 0.25:1 (i.e., ranging from (0.0001:1 or 0.0001/[1+0.0001]=0.01 percent up to 0.25:1 or 0.25/[1+0.25]=20 percent). Thus, the broad range (0.01 to 20 percent) overlaps the numerical range of claim 1 (polynucleotide-containing species constitutes at least 5 percent of the total weight of the microparticles), overlaps the numerical range of claim 27 (polynucleotide-containing species constitutes 10 to 30 percent of the total weight of the microparticles) and embraces the numerical range of claims 28, 91 and 93 (polynucleotide-containing species constitutes 10 to 20 percent of the total weight of the microparticles).

For the intermediate range, however, the high "macromolecule" concentration is nearly two orders of magnitude (91 times) higher than the low macromolecule concentration. For the broad range, the high "macromolecule" concentration is more than three orders of magnitude (2500 times) higher than the low macromolecule concentration.

In this regard, it was held by the Federal Circuit in *Atofina, supra*, that a much narrower disclosure of 100-500 degrees C by a prior art reference did not describe the claimed range of 330-450 degrees C with sufficient specificity to be anticipatory. This was true even though the claimed range was *completely embraced* by the wide range taught in the reference. Moreover, the disclosure of an even narrower range of 150-350 degrees C by the prior art reference was not sufficient for anticipation of the claimed range of 330-450 degrees C in *Atofina*, even though the disclosed 350 degree endpoint of the narrower range was embraced by the claimed range.

Moreover, whereas the prior art and claimed ranges in *Atofina* were based on an "apples-to-apples" comparison (i.e., degrees C vs. degrees C), in the present case the comparison is more of a "fruit-to-apples" comparison, if you will (i.e., macromolecule vs. polynucleotide-containing species).

In the Office Action of December 23, 2008, the Examiner responds as follows: "While Applicant is right in pointing out that the values of 0.01:1 to 0.05:1 are not the same as the

claimed 5% and 10% values, O'Hagan also teaches a polynucleotide to microparticle ratio of 0.25:1 (see column 14, lines 1-10), i.e., the polynucleotide constitutes 20% of the total weight of the microparticles. Since MPEP states that patents are relevant art for all they contain, by teaching that the polynucleotide constitutes 20% of the total weight of the microparticles, O'Hagan anticipates the values of at least 5% (claim I), 10 to 30% (claim 27), and 10 to 20% (claims 28, 91, and 93)."

However, even assuming for the sake of argument that the O'Hagan specification had happened to explicitly teach microparticles with adsorbed *polynucleotide* (rather than macromolecule) having a weight to weight ratio of from 0.0001:1 to 0.25:1 *polynucleotide* to microparticles (i.e., 0.01 to 20 percent *polynucleotide*), it remains the case that the Examiner is erroneously treating the 20 percent value as if it were specific example. It is not. Rather, it is the endpoint of a range.

As noted in *Atofina supra* "the disclosure of a range is no more a disclosure of the end points of the range than it is each of the intermediate points." For this reason, the disclosed ranges of 150-350 degrees C and 100-500 degrees C were held not to anticipate the claimed range of 330-450 degrees C in *Atofina*. As in *Atofina*, in the present case, an allegedly disclosed range of 0.01 to 20 percent polynucleotide does not anticipate a claimed range of 5 percent or more (claim 1), a claimed range of 10 to 20 percent (claims 28, 91 and 93) or a claimed range of 10 to 30 percent (claim 27).

The Examiner further states the following at pages 10-11 of the Office Action of December 23, 208: "Applicant argues that Atofina makes clear that the endpoint of a range is not a specific example. This argument is not found persuasive because in Atofina the claimed range was 330-450°C without specifically reciting the value of 350°C which is the endpoint value of the range of 150-350°C disclosed by the art. In the instant case, the claims specifically recite the endpoint of 20% and O'Hagan specifically discloses a range having the endpoint value of 20%; therefore, O'Hagan anticipates the claimed 20% (or at least 5%) value."

In the Examiner interview of April 7, 2009, the Examiner recognized that the 0.25:l value was an endpoint of a range. The Examiner urged, however, that the present fact pattern was distinguishable from *Atofina*, because in *Atofina*, the *endpoints* of the claimed range (330-450 degrees C) didn't not correspond to any of the *endpoints* in the reference (100-500 degrees C, more preferably, 150-350 degrees C), whereas in the present application, an endpoint of one of

the ranges claimed (i.e., 20 percent in claims 28, 91, 93) did correspond to an endpoint in the reference.

In rebuttal, several points should be made. First, the MPEP clearly indicates that the "sufficient specificity" test of *Atofina* is applicable to situations where the prior art discloses a range which "***touches*** … the claimed range". See MPEP 2131.03 II (emphasis added). Consequently, the holding in *Atofina* that "the disclosure of a range is no more a disclosure of the end points of the range than it is each of the intermediate points" applies to the instant case. The Examiner, on the other hand, is clearly treating the endpoint as if it were a specific example in spite of the holding in *Atofina*: "the claims specifically recite the endpoint of 20% and O'Hagan specifically discloses a range having the endpoint value of 20%; therefore, O'Hagan anticipates the claimed 20% (or at least 5%) value."

In essence, the Examiner is attempting to distinguish the fact pattern in *Atofina* by urging that the present fact pattern, in which the endpoint disclosed in O'Hagan *is the same as* the endpoint of certain claimed ranges, is somehow more compelling than the fact pattern in *Atofina,* wherein the endpoint disclosed in the prior art *fell squarely within* the claimed range. In fact, the present fact pattern is more favorable to the Applicant.

In *Atofina,* a disclosed endpoint fell squarely within a claimed range, yet did not anticipate the claimed range. To argue that the court in *Atofina* would have, on the other hand, found anticipation had the disclosed endpoint merely touched the claimed endpoint is not logical. In other words, the argument that if the claimed range had been *350*-450 degrees C in *Atofina*, rather than 330-450 degrees C (a narrower claimed range), the claimed range would have been anticipated by the disclosed range of 150-350 degrees C, simply because the endpoints matched, is a *non sequitur*. Yet that is, in essence, what the Examiner appears to be saying when she urges that because the claims specifically recite an endpoint of 20% and because O'Hagan specifically discloses an endpoint value of 20%, O'Hagan anticipates the claimed 20% value.

Again, the Examiner's position arises from the Examiner focusing on the fact that O'Hagan describes microparticles with adsorbed macromolecules having a weight to weight ratio of 0.25:1, while ignoring the fact that this ratio is set forth in O'Hagan as an *endpoint* of a range rather than an independent value, thereby ignoring the holding in *Atofina.*

For at least the foregoing reasons, it is respectfully submitted that the claimed amounts of adsorbed polynucleotide-containing species are not disclosed with "sufficient specificity" to constitute an anticipation of the claims.

Cationic Detergent

With respect to cationic detergent, the reasons for why O'Hagan falls short of being an anticipatory reference are analogous to those set forth above in conjunction with the claimed polynucleotide-containing species.

Claim 52 sets forth a process in which a w/o/w emulsion is formed that comprises polymer and cationic surfactant, wherein the weight-to-weight surfactant-to-polymer ratio is in the range of from 0.0025:1 to about 0.05:1.

O'Hagan teaches that "a weight to weight detergent to polymer ratio in the range of from about 0.00001:1 to about 0.1:1 will be used, more preferably from about 0.0001:1 to about 0.01:1, more preferably from about 0.001:1 to about 0.01:1, and even more preferably from about 0.005:1 to about 0.01:1." See col. 13, lines 32-37.

Note that this passage pertains generally to "detergents," which are defined at col. 5, lines 28-36 to "include surfactants and emulsion stabilizers. Anionic detergents include, but are not limited to, SDS, SLS, sulphated fatty alcohols, and the like. Cationic detergents include, but are not limited to, cetrimide (CTAB), benzalkonium chloride, DDA (dimethyl dioctodecyl ammonium bromide), DOTAP, and the like. Nonionic detergents include, but are not limited to, sorbitan esters, polysorbates, polyoxyethylated glycol monoethers, polyoxyethylated alkyl phenols, poloxamers, and the like."

To the extent that these ranges embrace the ranges of method claim 52, they are not sufficiently specific to constitute anticipation under the statute and the case law. See *Atofina supra.* As above, it should be reemphasized that whereas the prior art and claimed ranges in *Atofina* were based on an "apples-to-apples" comparison (i.e., degrees C vs. degrees C), in the present case the comparison is more of a "fruit-to-apples" comparison (i.e., detergents vs. cationic detergent).

With regard to the specific examples in O'Hagan, in Example 2 of O'Hagan, 12.5 ml of a 4% PLG solution (which contains 0.5 g PLG) and a 50 ml of a 0.5% CTAB solution (which contains 0.25 g CTAB) are employed, corresponding to 50% CTAB relative to PLG, or a weight-

to-weight surfactant-to-polymer ratio of 0.5:1. These percentages are much greater that the range of cationic surfactant used in claim 52. See also Example 1 of the present specification, wherein 16.6 ml of a 6 % PLG solution (which contains 1 g PLG) and a solution containing 10 mg CTAB are employed, corresponding to a mere 1% CTAB relative to PLG. A repeat procedure employed a mere 4% CTAB relative to PLG.

Note also that the 50% CTAB relative to PLG used in producing the microparticles of O'Hagan is outside even the broadest weight to weight detergent to polymer ratio range described in O'Hagan (i.e., a range of from about 0.00001:1 to about 0.1:1). It is recognized, however, that the microparticles produced by O'Hagan using 50% CTAB relative to PLG are washed with water by centrifugation four times, which would have reduced the CTAB content. As indicated in Singh et al., *Proc. Natl. Acad. Sci. USA*, 2000, 97:811-816 (of record) at page 815, right column, third paragraph, washing twice with water by centrifugation results in a CTAB level of 4 micrograms of CTAB per milligram of PLG polymer, or a CTAB concentration of 0.4% relative to PLG. The amount of CTAB in the microparticles of Example 2 of O'Hagan, which were washed four times (rather than two) would be at least as low, given that the same relative amount of CTAB was used to form the microparticles of O'Hagan as was used in Singh.

Unlike O'Hagan, the microparticles in claims 1 and 52 are not washed to remove cationic surfactant subsequent to microparticle formation. This is also true of the microparticles of Examples 1 and 2 in the present specification--consequently, the same amount of detergent used to form the microparticles (1% and 4% CTAB relative to PLG) is also present in the microparticles to which the DNA was adsorbed.

Moreover, in O'Hagan, even though 50% CTAB relative to PLG was used in producing the microparticles, the amount of detergent in the microparticles to which the DNA is adsorbed is far less, specifically, not more than 0.4% CTAB relative to PLG, for the reasons discussed above. This amount is less than the amount of cationic detergent in claims 97-99 and 101.

For at least these reasons, reconsideration and withdrawal of claim rejection under 35 USC §102(e) are requested.

CONCLUSION

Applicant submits that this application is in condition for allowance, early notification of which is earnestly solicited. The Examiner is encouraged to contact the undersigned at (703) 433-0510 to discuss any outstanding issues in this case.

FEES

The Office is authorized to charge any fees that are due as a result of this Response, and to credit any overpayments, to the undersigned attorney's PTO Deposit Account #50-1047.

CORRESPONDENCE

Please direct all correspondence to:

Novartis Vaccines and Diagnostics, Inc.
Intellectual Property Department-X100B
P.O. Box 8097
Emeryville, CA 94662-8097.

Respectfully submitted,

/David B. Bonham/

David B. Bonham
Registration No. 34,297

Attorney for Applicant
Mayer & Williams, PC
251 North Avenue West, 2nd Floor
Westfield, NJ 07090
Tel.: 703-433-0510
Fax: 703-433-2362